

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Evans and Blumberg Art Unit: 1631
Application No.: 09/458,366 Examiner Unassigned
Filed: December 9, 1999
Title: NOVEL STEROID-ACTIVATED NUCLEAR RECEPTORS AND USES
THEREFOR

Assistant Commissioner of Patents
Washington, D.C. 20231

TRANSMITTAL SHEET

Sir:

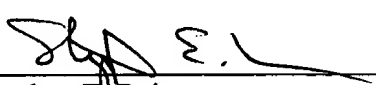
Transmitted herewith for the above-identified application please find:

1. Information Disclosure Statement;
2. Copy of Form PTO-1449 from co-pending application; and
3. Postcard.

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any fee to Deposit Account No. 07-1895. A duplicate copy of this Transmittal Sheet is attached.

Respectfully submitted,

Dated: 5/6/00


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Telephone: (858) 677-1409
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GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1600
San Diego, CA 92121-2189

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INFORMATION DISCLOSURE STATEMENT

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Sir:

In accordance with 37 C.F.R. 1.97, Applicants submit for consideration by the Examiner references relating to the above-identified application. For the convenience of the Examiner, these references are listed on the attached Forms PTO-1449 that were filed in co-pending U.S. Application Serial No. 09/227,718, filed January 8, 1999, of which this application is a continuation-in-part application. Copies of the references are not provided herewith since a copy of each was provided in the parent application.

It is respectfully requested that these references be considered in the examination of this application and their consideration be made of written record in the application file.

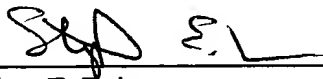
In re Application of:
Evans and Blumberg
Application No.: 09.458,366
Filed: December 9, 1999
Page 2

PATENT
Attorney Docket No.: SALK2270-2

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 07-1895.

Respectfully submitted,

Dated: 5/8/00



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Enc. Forms 1449 (SALK2270-1)

| | | |
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| FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office | Docket No. SALK2270-1 | Serial No.: 09/227,718 |
| | Applicant(s): Ronald M. Evans | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT | Filing Date: January 8, 1999 | Group Art Unit: 1643 |

U.S. PATENT DOCUMENTS

| EXAM. INITIALS | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB- CLASS | FILED DATE |
|-------------------|----|--------------------|----------|-----------------|-------|---------------|---------------|
| | AA | 4,160,152 | 07/03/79 | Wightman et al. | 219 | 438 | 12/04/78 |
| | AB | 4,256,108 | 03/17/81 | Theeuwes | 128 | 260 | 05/21/79 |
| | AC | 4,265,874 | 05/05/81 | Bonsen et al. | 424 | 15 | 04/25/80 |

FOREIGN PATENT DOCUMENTS

| EXAM. INITIALS | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB- CLASS | TRANSLATIO N (YES/NO) |
|-------------------|--|--------------------|------|---------|-------|---------------|-----------------------------|
| | | NONE | | | | | |

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages)

| | | |
|--|----|--|
| | AD | Adlercreutz and Mazur, "Phyto-oestrogens and Western Diseases," <i>Ann. Med.</i> , 29:95-120 (1997) |
| | AE | Altschul et al., "Basic Local Alignment Search Tool," <i>J Mol. Biol.</i> , 215:403-410 (1990) |
| | AF | Baes et al., "A New Orphan Member of the Nuclear Hormone Receptor Superfamily That Interacts with a Subset of Retinoic Acid Response Elements," <i>Molecular and Cellular Biology</i> , 14(3):1544-1552 (1994) |
| | AG | Bahouth et al., "Immunological approaches for probing receptor structure and function," <i>TIPS/Reviews</i> , 12:338-343 (1991) |
| | AH | Bammel et al., "Divergent effects of different enzyme-inducing agents on endogenous and exogenous testosterone," 42:641-644 (1992) |

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| | Applicant(s): Ronald M. Evans | |
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|----|---|
| AI | Barwick et al., "Trans-species Gene Transfer for Analysis of Glucocorticoid-Inducible Transcriptional Activation of Transiently Expressed Human CYP3A4 and Rabbit CYP3A6 in Primary Cultures of Adult Rat and Rabbit Hepatocytes," <i>Molecular Pharmacology</i> , 50:10-16 (1996) |
| AJ | Beato et al., "Steroid Hormone Receptors: Many Actors in Search of a Plot," <i>Cell</i> , 83:851-857 (1995) |
| AK | Beaune et al., "Isolation and sequence determination of a cDNA clone related to human cytochrome P-450 nifedipine oxidase," <i>Proc. Natl. Acad. Sci.</i> , 83:8064-8068 (1986) |
| AL | Blumberg et al., "Novel retinoic acid receptor ligands in <i>Xenopus</i> embryos," <i>Proc. Natl. Acad. Sci.</i> , 93:4873-4878 (1996) |
| AM | Blumberg et al., "BXR, an embryonic orphan nuclear receptor activated by a novel class of endogenous benzoate metabolites," <i>Genes & Development</i> , 12:1269-1277 (1998) |
| AN | Burger et al., "Paradoxical transcriptional activation of rat liver cytochrome P-450 3A1 by dexamethasone and the antiglyucocorticoid pregnenolone 16 α -carbonitrile: Analysis by transient transfection into primary monolayer cultures of adult rat hepatocytes," <i>Proc. Natl. Acad. Sci. (USA)</i> , 89:2145-2149 (1992) |
| AO | Denison and Whitlock, "Xenobiotic-inducible Transcription of Cytochrome P450 Genes," <i>Journal of Biological Chemistry</i> , 270(31):18175-18178 (1995) |
| AP | Devereux et al., "A comprehensive set of sequence analysis programs for the VAX," <i>Nucleic Acids Research</i> , 12:387-395 (1984) |
| AO | Edwards et al., "Changes in Cortisol Metabolism Following Rifampicin Therapy," <i>The Lancet</i> , 2:549-551 (1974) |
| AR | Elshourbagy and Guzelian, "Separation, Purification, and Characterization of a Novel Form of Hepatic Cytochrome P-450 from Rats Treated with Pregnenolone-16 α -carbonitrile," <i>Journal of Biological Chemistry</i> , 255:1279-1285 (1980) |
| AS | Enmark and Gustafsson, "Orphan Nuclear Receptors - The First Eight Years," <i>Mol. Endo.</i> , 10(11):1293-1307 (1996) |

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| AT | Evans, Ronald M., "The Steroid and Thyroid Hormone Receptor Superfamily," <i>Science</i> , 240:889-895 (1988) |
| AU | Fernandez-Salguero and Gonzalez, "The CYP2A gene subfamily: species differences, regulation, catalytic activities and role in chemical carcinogenesis," <i>Pharmacogenetics</i> , 5:S123-S128 (1995) |
| AV | Forman et al., "Unique Response Pathways Are Established by Allosteric Interactions among Nuclear Hormone Receptors," <i>Cell</i> , 81:541-550 (1995) |
| AW | Forman et al., "Hypolipidemic drugs, polyunsaturated fatty acids, and eicosanoids are ligands for peroxisome proliferator-activated receptors α and δ ," <i>Proc. Natl. Acad. Sci. USA</i> , 94:4312-4317 (1997) |
| AX | Gonzalez et al., "Complete cDNA and Protein Sequence of a Pregnenolone 16 α -Carbonitrile-induced Cytochrome P-450," <i>Journal of Biological Chemistry</i> , 260(12):7435-7441 (1985) |
| AY | Gonzalez et al., "Pregnenolone 16 α -Carbonitrile-Inducible P-450 Gene Family: Gene Conversion and Differential Regulation," <i>Molecular and Cellular Biology</i> , 6(8):2969-2976 (1986) |
| AZ | Gonzalez, Frank J., "Human cytochromes P450: problems and prospects," <i>TIPS Reviews</i> , 13:346-352 (1992) |
| BA | Gottlicher et al., "Fatty acids activate a chimera of the clofibric acid-activated receptor and the glucocorticoid receptor," <i>Proc. Natl. Acad. Sci. USA</i> , 89:4653-4657 (1992) |
| BB | Guengerich, F. Peter, "Metabolism of 17 α Ethynylestradiol in Humans", <i>Life Sciences</i> , 47:1981-1988 (1990) |
| BC | Hankinson, Oliver, "The Aryl Hydrocarbon Receptor Complex," <i>Annu. Rev. Pharmacol. Toxicol.</i> 35:307-340 (1995) |
| BD | Hardwick et al., "Cloning of DNA Complementary to Cytochrome P-450 Induced by Pregnenolone-16 α carbonitrile," <i>Journal of Biological Chemistry</i> , 258:10182-10186 (1983) |

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| BE | Henikoff and Henikoff, "Amino acid substitution matrices from protein blocks," <i>Proc. Natl. Acad. Sci. USA</i> , 89 :10915-10919 (1992) |
| BF | Heuman et al., "Immunochemical Evidence for Induction of a Common Form of Hepatic Cytochrome P-450 in Rats Treated with Pregnenolone-16 α -carbonitrile or other Steroidal or Non-Steroidal Agents," <i>Molecular Pharmacology</i> , 21 :753-760 (1982) |
| BG | Hollenberg et al., "Primary structure and expression of a functional human glucocorticoid receptor cDNA," <i>Nature</i> , 318(6047) :635-641 (1985) |
| BH | Hollenberg et al., "Colocalization of DNA-Binding and Transcriptional Activation Functions in the Human Glucocorticoid Receptor," <i>Cell</i> , 49 :39-46 (1987) |
| BI | Holtbecker et al., "The Nifedipine-Rifampin Interaction: Evidence for Induction of Gut Wall Metabolism," <i>Drug Metabolism and Disposition</i> , 23(10) :1121-1123 (1996) |
| BI | Jonat et al., "Antitumor Promotion and Antiinflammation: Down-Modulation of AP-1 (Fos/Jun) Activity by Glucocorticoid Hormone," <i>Cell</i> , 62 :1189-1204 (1990) |
| BK | Juchau, M.R., "Substrate Specificities and Functions of the P450 Cytochromes," <i>Life Sciences</i> , 47 :2385-2394 (1990) |
| BL | Kliwer et al., "Fatty acids and eicosanoids regulate gene expression through direct interactions with peroxisome proliferator-activated receptors α and γ ," <i>Proc. Natl. Acad. Sci. USA</i> , 94 :4318-4323 (1997) |
| BM | Kliwer et al., "An Orphan Nuclear Receptor Activated by Pregnanes Defines a novel Steroid Signaling Pathway," <i>Cell</i> , 92 :73-82 (1998) |
| BN | Kolars et al., "First-pass metabolism of cyclosporin by the gut," <i>Lancet</i> , 338 :1488-1490 (1991) |
| BO | Kolars et al., "Identification of Rifampin-inducible P450III _{A4} (CYP3A4) in Human Small Bowel Enterocytes," <i>Journal of Clinical Investigation, Inc.</i> , 90 :1871-1878 (1992) |
| BP | Kyriazopoulou et al., "Rifampicin-Induced Adrenal Crisis In Addisonian Patients Receiving Corticosteroid Replacement Therapy," <i>Journal of Clinical Endocrinology and Metabolism</i> , 59(6) :1204-1206 (1984) |

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| BQ | Kyriazopoulou and Vagenakis, "Abnormal Overnight Dexamethasone Suppression Test in Subjects Receiving Rifampicin Therapy," <i>Journal of Clinical Endocrinology and Metabolism</i> , 74(1) :315-317 (1992) |
| BR | Ladiaz and Karathanasis, "Regulation of the Apolipoprotein AI Gene by ARP-1 a Novel Member of the Steroid Receptor Superfamily," <i>Science</i> , 251 :561-565 (1991) |
| BS | Lee et al., "Time course of the changes in prednisolone pharmacokinetics after co-administration or discontinuation of rifampin," <i>Eur. Journal of Clinical Pharmacology</i> , 45 :287-289 (1993) |
| BT | Li and Evans, "Ligation independent cloning irrespective of restriction site compatibility," <i>Nucleic Acids Research</i> , 25 :4165-4166 (1997) |
| BU | Lonning et al., "Plasma Levels of Estradiol, Estrone, Estrone Sulfate and Sex Hormone Binding Globulin in Patients Receiving Rifampicin," <i>J. Steroid Biochem.</i> , 33(4A) :631-635 (1989) |
| BV | Mangelsdorf et al., "The Nuclear Receptor Superfamily: The Second Decade," <i>Cell</i> , 83 :835-839 (1995) |
| BW | Mangelsdorf and Evans, "The RXR Heterodimers and Orphan Receptors," <i>Cell</i> , 83 :841-850 (1995) |
| BX | McAllister et al., "Rifampicin reduces effectiveness and bioavailability of prednisolone," <i>British Medical Journal</i> , 286 :923-925 (1983) |
| BY | Miyata et al., "Transcriptional Elements Directing a Liver-Specific Expression of P450/6 β A (CYP3A2) Gene-Encoding Testosterone 6 β -Hydroxylase," <i>Archives of Biochemistry and Biophysics</i> , 318(1) :71-79 (1995) |
| BZ | Molowa et al., "Complete cDNA sequence of a cytochrome P-450 inducible by glucocorticoids in human liver," <i>Proc. Natl. Acad. Sci. USA</i> , 83 :5311-5315 (1986) |
| CA | Nebert, Daniel W., "P450 Genes: Structure, Evolution, and Regulation," <i>Ann. Rev. Biochem.</i> , 56 :945-993 (1987) |

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| CB | Needleman and Wunsoh, "A General Method Applicable to the Search for Similarities in the Amino Acid Sequence of Two Proteins," <i>Journal of Molecular Biology</i> , 48 :443-453 (1970) |
| CC | O'Malley and Conneely, "Orphan Receptors: In Search of a Unifying Hypothesis for Activation," <i>Molecular Endocrinology</i> , 6 :1359-1361 (1992) |
| CD | Ogura and Evans, "A retinoic acid-triggered cascade of HOXB1 gene activation," <i>Proc. Natl. Acad. Sci. USA</i> , 92 :387-391 (1995) |
| CE | Ohnhaus et al., "Urinary Excretion of 6 β -Hydroxycortisol and the Time Course Measurement of Enzyme Induction in Man," <i>Eur. J. Clin. Pharmacol.</i> , 36 :39-46 (1989) |
| CF | Quattrochi et al., "A Novel cis-Acting Element in a Liver Cytochrome P450 3A Gene Confers Synergistic Induction by Glucocorticoids plus Antiglucocorticoids," <i>Journal of Biological Chemistry</i> , 270 (48):28917-28923 (1995) |
| CG | Russel and Wilson, "Steroid 5 α -Reductase: Two Genes/Two Enzymes," <i>Annu. Rev. Biochem.</i> , 63 :25-61 (1994) |
| CH | Schuetz and Guzelian, "Induction of Cytochrome P-450 by Glucocorticoids in Rat Liver," <i>Journal of Biological Chemistry</i> , 259 (3):1999-2006 (1984) |
| CJ | Schuetz and Guzelian, "Induction of Cytochrome P-450 by Glucocorticoids in Rat Liver," <i>Journal of Biological Chemistry</i> , 259 (3):2007-2012 (1984) |
| CJ | Schule et al., "Functional Antagonism between Oncoprotein c-Jun and the Glucocorticoid Receptor," <i>Cell</i> , 62 :1217-1226 (1990) |
| CK | Selye, H., "Hormones and Resistance," <i>Journal of Pharmaceutical Sciences</i> , 60 (1):1-28 (1971) |
| CG | Sucov et al., "Characterization of an autoregulated response element in the mouse retinoic acid receptor type β gene," <i>Proc. Natl. Acad. Sci. USA</i> , 87 :5392-5396 (1990) |
| CM | Staden, Rodger, "The current status and portability of our sequence banding software," <i>Nucleic Acids Research</i> , 14 (1):217-231 (1986) |

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| | CN | Terzolo et al., "Misdiagnosis of Cushing's Syndrome in a Patient Receiving Rifampicin Therapy for Tuberculosis," <i>Horm. Metab. Res.</i> , 27 :148-150 (1995) |
| | CO | Umesono et al., "Direct Repeats as Selective Response Elements for the Thyroid Hormone, Retinoic Acid, and Vitamin D ₃ Receptors," <i>Cell</i> , 65 :1255-1266 (1991) |
| | CP | Watkins et al., "Erythromycin Breath Test as an Assay of Glucocorticoid-inducible Liver Cytochromes P-450," <i>J. Clin. Invest.</i> , 83 :688-697 (1989) |
| | CQ | Wietholtz et al., "Stimulation of bile acid 6 α -hydroxylation by rifampin," <i>Journal of Hepatology</i> , 24 :713-718 (1996) |
| | CR | Willy et al., "LXR, a nuclear receptor that defines a distinct retinoid response pathway," <i>Genes & Development</i> , 9 :1033-1045 (1995) |
| | CS | Wurtz et al., "A canonical structure for the ligand-binding domain of nuclear receptors," <i>Nature Structural Biology</i> , 3 :87-94 (1996) |
| | CT | Yang-Yen et al., "Transcriptional Interference between c-Jun and the Glucocorticoid Receptor: Mutual Inhibition of DNA Binding Due to Direct Protein-Protein Interaction," <i>Cell</i> , 62 :1205-1215 (1990) |
| | CU | Zawawi et al., "The Effects of Therapy with Rifampicin and Isoniazid on Basic Investigations for Cushing's Syndrome," <i>Ir. j. Med. Sci.</i> , 165 :300-302 (1996) |

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